sequence MF α of *S. cerevisiae* that is a peptide comprised of 13 amino acid residues may be employed. The MF α signal sequence has a protease site determined by the sequence of amino acids Lys-Arg-Glu-Ala (SEQ ID NO:26). During the cloning process in pPIC9 of a human insulin precursor gene, this gene may be preferably inserted into the site Xho I that eliminates the –Glu-Ala- residues, whereby the starting insert of the human insulin gene is maintained immediately after the proteases removal site (Figure 1). The cloning in site Xho I permits to obtain a precursor released into the culture medium without remaining amino acids belonging to the signal peptide, thus simplifying the steps of purification of the human insulin. --

Replace lines 3-19 at page 41 with the following text.

--**Primers:**

SEQ ID NO:1: 5′-TCACACCTGG TGGAAGCTCT CTACCTAGTG TGCGGG -3′

SEQ ID NO:2: 5′-GGTCTTGGGT GTGTAGAAGA AGCCTCGTTC CCCGCACACT AGGTA-3′

SEQ ID NO:3: 5′- TTTGTGAACC AACACCTGTG CGGCTCACAC CTGGTGGAA -3′

SEQ ID NO:4: 5′-GCTGGTACAG CATTGTTCCA CAATGCCACG CTTGGTCTTG GGTGT -3′

SEQ ID NO:5: 5′-CTAGTTGCAG TAGTTCTCCA GCTGGTAGAG GGAGCAGATG CTGGTACAGC AT-3′

Final Product:

SEQ ID NO:6: 5′- TTTGTGAACC AACACCTGTG CGGCTCACAC CTGGTGGAAG CTCTCTACCT AGTGTGCGGG GAACGAGGCT TCTTCTACAC ACCCAAGACC AAGCGTGGCA TTGTGGAACA ATGCTGTACC AGCATCTGCT CCCTCTACCA GCTGGAGAAC TACTGCAACT AG -3′

(complete insulin precursor) --

Replace lines 1-21 at page 42 with the following text.

--Construction of an insulin precursor by the polymerase chain reaction (PCR) with the codons more utilized by Pichia pastoris.

Primers:

SEQ ID NO:7: 5′-ACTTGGTTGA AGCTTTGTAC TTGGTTTGTG GTGAAAGAGG TTTCTTCTAC-3′

SEQ ID NO:8: 5′-AGAAGTACAA CATTGTTCAA CGATACCTCT CTTAGTCTTT GGAGTGTAGA -3′

SEQ ID NO:9: 5′-ACACTTGTGT GGTTCTCACT TGGTTGAAGC TTT-3′

SEQ ID NO:10: 5′- TTACTCGAGT TAGTTACAGT AGTTTTCCAA TTGGTACAAA GAACAGATAG AAGTACAACA TTGTTC -3′

SEQ ID NO:11: 5′-CCGCTCGAGA AGAGATTTGT TAACCAACAC TTGTGT -3′

The obtained product contains the following sequence:

SEQ ID NO:12:

5′-TTTGTTAACC AACACTTGTG TGGTTCTCAC TTGGTTGAAG CTTTGTACTT GGTTTGTGGT GAAAGAGGTT TCTTCTACAC TCCAAAGACT AAGAGAGGTA TCGTTGAACA ATGTTGTACT TCTATCTGTT CTTTGTACCA ATTGGAAAAC TACTGTAACT AA-3′--

Replace lines 12-20 at page 43 with the following text.

--Example 3

Construction of Factor α with preferences codons of Pichia pastoris

By means of this technique the nucleotide sequence corresponding to the leader sequence or signal peptide was cloned.

The employed primers were the following:

SEQ ID NO:13: 5′-CGCGGATCCA AACCATGAGA TTCCCATCTA TCTTCACTGC TGTTTTGTTC GCTGCT -3′--

Replace lines 1-16, at page 44 with the following text.

--SEQ ID NO:14: 5′- GTTTTGTTCG CTGCTTCTTC TGCTTTGGCT GCTCCTGTTA ACACTACTAC TGAAGACGAA ACTGCTCA-3′

SEQ ID NO:15: 5′-ACGTCGAAGT CACCTTCCAA GTCAGAGTAA CCGATAACCG CTTCAGCTGG GATTTGAGCA GTTTCGTCTT C -3′

SEQ ID NO:16: 5′-GATGAACAAC AAACCATTAT TAGTAGAGTT AGAGAAAGGC AAAACAGCAA CGTCGAAGTC ACCTTC -3′

SEQ ID NO:17: 5′-CCGCTCGAGA GAAACACCCT CTTCCTTAGC AGCGATAGAA GCGATAGTAG TGTTGATGAA CAACAAACCA TT -3′

The final product has the following sequence:

SEQ ID NO:18

5′-ATGAGATTCC CATCTATCTT CACTGCTGTT TTGTTCGCTG CTTCTTCTGC TTTGGCTGCT CCTGTTAACA CTACTACTGA AGACGAAACT GCTCAAATCC CAGCTGAAGC GGTTATCGGT TACTCTGACT TGGAAGGTGA CTTCGACGTT GCTGTTTTGC CTTTCTCTAA CTCTACTAAT AATGGTTTGT TGTTCATCAA CACTACTATC GCTTCTATCG CTGCTAAGGA AGAGGGTGTT TCTCTCGAGA AGAGAGAGGC TGAAGCA-3′--

Replace lines 7-23 at page 45 with the following text.

--3- The PCR product SEQ ID NO:18 was digested with the same restriction enzymes utilized in 1 and was ligated to the fragment obtained in 2.

4- The vector obtained in 3 and the PCR fragment SEQ ID NO:12 was digested with the XhoI, and subsequently they were ligated.

5- The recombinants having the correct orientation of the insulin precursor insert were detected by the HpaI.

EXAMPLE 4

Cloning of insulin precursor gene in pPIC9 yeasts vector

The DNA fragment encoding the insulin precursor was amplified by PCR, employing as a template SEQ ID NO:6 previously obtained and as primers the following sequences:

SEQ ID NO:19: 5′ -GGGGATCCAT ATGCTCGAGA AAAGATTTGT GAACCAACAC CTGT-3′.--

Replace lines 1-2 at page 46 with the following text.

--SEQ ID NO:20: 5′ -TTAGAATTCC CGGGTCTAGT TGCAGTAGTT CT– 3′.--

Replace lines 1-4 at page 49 with the following text.

--SEQ ID NO:19: 5′ - GGGGATCCAT ATGCTCGAGA AAAGATTTGT GAACCAACAC CTGT-3′

SEQ ID NO:21: 5′-TCACTCGAGC GGTCTAGTTG CAGTAGTTCT-3′--

Replace lines 16-20 at page 58 with the following text.

--His probe that is a fragment 1587 bp of HIS4 gene obtained by digestion of vector Ppic9 with the MscI and the Ins probe that is a fragment 227 bp obtained by PCR employing as a

template the plasmid pPIC9IB and the primers corresponding to the sequences SEQ ID NOS:19 and 20.--

Replace lines 11-13 at page 62 with the following text.

--Sequence of primers:

5′ AOX I: 5′ - GACTGGTTCC AATTGACAAG C (SEQ ID NO:25)

3′AOX IN: 5′ - GTCGTGGTTT CTCATAGTAG AGTGGAC (SEQ ID NO:22)--

Replace lines 24-25 at page 63 with the following text.

--Gap primers:

Gap5': 5′ GGT CAT CAC TGC TCC AT (SEQ ID NO:23)--

Replace lines 1 at page 64 with the following text.

--Gap3′: 5′ AGC AGC ACC AGT GGA AGA (SEQ ID NO:24)--

Replace lines 17-20 at page 64 with the following text.

--Insulin precursor primers:

SEQ ID NO:19: 5′- GGGGATCCAT ATGCTCGAGA AAAGATTTGT GAACCAACAC CTGT

SEQ ID NO:21: 5′- TCACTCGAGC GGTCTAGTTG CAGTAGTTCT--